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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,452	09/09/2005	Eveline S.J.M. De Bont	ON/4-32717A	3044

1095 7590 09/05/2007

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
WEBB, WALTER E	

ART UNIT	PAPER NUMBER
1609	

MAIL DATE	DELIVERY MODE
09/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,452	DE BONT ET AL.	
	Examiner	Art Unit	
	Walter E. Webb	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/22/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-15 are pending and rejected.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 13 and 15 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

For the purposes of examination claims 13 and 15 will be treated as product claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 13 and 15 provide for the use of a pharmaceutical composition or a compound, but, since the claim does not set forth any steps involved in the

method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

For the purposes of examination claims 13 and 15 will be treated as product claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Wood et al., (WO 0241882).

Applicant's invention is drawn to a pharmaceutical composition, and a commercial package containing a compound of formula I, and a conventional compound or compound mixture useful in AML (acute myeloid leukemia) treatment and one pharmaceutically acceptable carrier (claims 8, 10, and 13-15), where a compound of formula I is PTK787 (claims 9 and 12), where the conventional compound can be a topoisomerase II inhibitor (claim 3), where the quantity is jointly therapeutically effective against AML (claim 11).

Wood et al. teach a method, a pharmaceutical composition, and a commercial package for treating angiogenesis, especially a proliferative disease, in a warm blooded animal, including leukemia. (See Abstract (57) on cover page; see also pg. 2, 3rd ¶.)

The compound of the method, pharmaceutical composition and commercial package is of formula I, as per claim 1 of the instant application, with every limitation therein. (See pp. 11-12.) The preferred compound of this formula is PTK787. (See pg. 12) Wood teaches combination of PTK787 with topoisomerase II inhibitors, antimetabolites etc. (see pg. 19 (bottom)). These compounds can be prepared for oral dosage form by any usual pharmaceutical media, such as water, glycols, oils, powders, capsules, tablets etc. (See pg. 10 1st para.) Solid pharmaceutical carriers are employed for tablets and capsules. (See ibid.) When administering a compound of formula I, i.e. PTK787, the dosage should be in range of about 150 to 4000mg/kg/day. (See pg. 21 4th para.) Wood also teaches a commercial package of their combination together with instructions for simultaneous, separate or sequential use thereof, as per claim 14. (See pg. 10 3rd para.)

The teachings of Wood reads on applicants claimed invention for treating AML, since AML is a proliferative disease characterized by rapid proliferation of abnormal cells which accumulate in the bone marrow.

It is well settled that the recitation of a new intended use for an old product does not make a claim to that old product patentable. See In re Spada, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990) ("The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from prior art, can not impart patentability to claims to the known composition."); Titanium Metals Corp. of Am. v. Banner, 778 F.2d 775, 782,227 USPQ 773, 778 (Fed. Cir. 1985) (composition claim reciting a newly discovered property of an old alloy did not satisfy

section 102 because the alloy itself was not new); In re Pearson, 494 F.2d 1399, 1403, 181 USPQ 641,644 (CCPA 1974) (intended use of an old composition does not render composition claim patentable). The intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. Since the composition of Wood is capable of performing the intended use of treating AML, then it meets the claims.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wood et al., (supra) in view of Klasa et al., (Hematology 2001), and in further view of De Bont et al., (Clinical Cancer Research 2002).

Applicant's invention is drawn to a method, a pharmaceutical composition, and a commercial package for treating a warm-blooded animal having acute myeloid leukemia (AML) by administering a compound of formula I, and a conventional compound or

compound mixture useful in AML treatment and one pharmaceutically acceptable carrier (claims 1, 8, 10, and 13-15), where a compound of formula I is PTK787 (claims 2, 9 and 12), where the conventional compound can be a topoisomerase II inhibitor, an antimetabolite, an antitumor antibiotic or a mixture of such compounds (claim 3), where the conventional compound can also be methotexate (claim 4), where the AML is resistant to conventional chemotherapy (claim 5), where the warm-blooded animal is a human (claim 6), where the human is a juvenile human (claim 7). Applicant also claims a pharmaceutical composition comprising a compound of formula I, and a conventional compound useful in AML treatment, where the quantity is jointly therapeutically effective against AML (claim 11).

Wood et al. teach a method, a pharmaceutical composition, and a commercial package for treating angiogenesis, especially a proliferative disease, in a warm blooded animal, especially a human, such as leukemia. (See Abstract (57) on cover page; see also pg. 2, 3rd ¶.) The compound of the method, pharmaceutical composition and commercial package is of formula I, as per claim 1 of the instant application, with every limitation therein. (See pp. 11-12.) The preferred compound of this formula is PTK787. (See pg. 12) Wood teaches combination of PTK787 with topoisomerase II inhibitors, antimetabolites etc. (see pg. 19 (bottom)), and methotexate, as per claim 4, (see pg. 20 1st para.). These compounds can be prepared for oral dosage form by any usual pharmaceutical media, such as water, glycols, oils, powders, capsules, tablets etc. (See pg. 10 1st para.) Solid pharmaceutical carriers are employed for tablets and capsules. (See ibid.) When administering a compound of formula I, i.e. PTK787, the

dosage should be in a range of about 150 to 4000mg/kg/day. (See pg. 21 4th para.) Methotexate may be administered at a dosage ranging from about 5 to 500 mg/m^{2}day. (See pg. 22.) Wood also teaches a commercial package of their combination together with instructions for simultaneous, separate or sequential use thereof, as per claim 14. (See pg. 10 3rd para.)

Wood does not teach that the leukemia is specifically acute myeloid leukemia (AML).

Klasa et al. teach that leukemic monocytes of AML secrete VEGF and display VEGF receptors. (See Hematologic Malignancies at pg. 450.) Klasa et al. introduces novel therapeutic strategies focusing on a molecular marker relevant to a particular malignancy. (See Abstract at p. 443.)

De Bont et al. teach that AML cells of juveniles also secrete VEGF and display VEGF receptors. (See Discussion at pg. 2860.)

It would have been obvious to a person of ordinary skill in the art at the time of applicant's invention to use the composition of Wood to treat AML since AML is a proliferative disease characterized by rapid proliferation of abnormal cells, which accumulate in the bone marrow, and Woods disclosed that PTK787 is a VEGF (vascular endothelial growth factor) receptor tyrosine kinase inhibitor which decreases the activity of VEGF. (See Wood disclosure, pg. 1, 1st and 2nd paragraphs.) By decreasing the activity of VEGF, PTK787 can reduce the proliferation of the malignant cells. Klasa teaches that, in AML, leukemic monocytes secrete VEGF and display

VEGF receptors. Therefore, it would have been obvious to treat AML, by decreasing the proliferation of the malignant cells of AML in Wood.

It would also have been obvious to a person of ordinary skill in the art at the time of applicant's invention to use the composition of Wood to treat AML in a juvenile since de Bont teaches that AML cells in children also secrete VEGF and display VEGF receptors. De Bont also concluded that intervention with VEGF inhibitors in AML patients could improve their outcome. (See Discussion at pg. 2860.)

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 9:00am-5:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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JEFFREY STUCKER
SUPERVISORY PATENT EXAMINER